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Hospitalizations for ketoacidosis in type 1 diabetes mellitus, 2008 to 2018

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ABSTRACT

The objective of this study was to characterize epidemiological trends, outcomes in hospitalized patients, and the disease burden of hospitalizations for diabetic ketoacidosis (DKA) in patients with type 1 diabetes mellitus (T1DM). This was a retrospective interrupted trends study involving hospitalizations for DKA in patients with T1DM in the US from 2008 to 2018 using data from the Nationwide Inpatient Sample. The total number of hospitalizations during each calendar year was obtained, and trends in inpatient mortality rate, mean length of hospital stay (LOS), and mean total hospital cost (THC) were calculated. Between 2008 and 2018, there was a trend toward increasing hospitalizations for T1DM with DKA (*P*-trend <0.001). Over the decade, there was a steady rise in the proportion of patients with a Charlson comorbidity index >1. There was no statistically significant change in adjusted inpatient mortality in patients with T1DM admitted for DKA over the study period despite an apparent trend of a decreasing crude mortality rate (*P*-trend $= 0.063$). There was a statistically significant decrease in both LOS and THC over the study period. In conclusion, there was a significant decrease in both LOS and THC, potentially reflecting improvements in the management of DKA in patients with T1DM.

KEYWORDS Cost of care; diabetes; mortality

Diabetic ketoacidosis (DKA) is a metabolic derangement that can occur in patients with type 1 diabetes mellitus (T1DM).[1] Over time, new guidelines have been established to encourage best practices, standardize care, and reduce morbidity and mortality.[1] In the last 20 years, mortality rates have been reported to have fallen significantly to <1%.[1] Improvements have been made in testing, technology, diagnosis, and monitoring.[1] Examining trends over time can help understand the effectiveness of interventions and improvements and guide future clinical practice. Thus, the goal of this study was to examine trends of the decade beginning in 2008 and ending in 2018 for hospitalization rates, mortality, and other outcome-related variables for DKA hospitalizations in patients with T1DM.

METHODS

This was a retrospective interrupted trends study involving hospitalizations principally for DKA in patients with T1DM in the US from 2008 to 2018. Data were sourced from the Nationwide Inpatient Sample (NIS), a large publicly available all-payer inpatient care database in the US, containing data on >7 million hospital stays per year. Its large sample size is ideal for developing national and regional estimates and enables analyses of rare conditions, uncommon treatments, and special populations for the studied years. The NIS was developed by the Healthcare Cost and Utilization Project (HCUP), a federal-state-industry partnership sponsored by the Agency for Healthcare Research and Quality. Billing data are submitted by hospitals to statewide data organizations across the US, covering more than 97% of the US population.[2] The NIS approximates a 20% stratified sample of discharges from US community hospitals, excluding rehabilitation and long-term acute care hospitals. This dataset is weighted to obtain national estimates.[3]

Databases prior to 2016 were coded using the International Classification of Diseases, Ninth Revision, Clinical Modification/Procedure Coding System (ICD-9-

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Table 1. Biodemographic characteristics of hospitalizations for diabetic ketoacidosis in patients with type 1 diabetes mellitus

Variables	2008	2010	2012	2014	2016	2018
Hospitalizations	79,129	91,897	104,090	119,335	109,930	116,710
Mean age (years)	34.9	35.2	35.3	36.1	34.2	34.4
Women	50.8%	50.5%	50.9%	50.7%	51.5%	50.2%
Race						
White	51.0%	52.0%	58.8%	58.4%	61.1%	60.4%
Black	17.2%	23.9%	22.2%	22.6%	21.7%	23.0%
Hispanic	7.7%	9.8%	9.9%	10.1%	9.6%	10.5%
Other	24.1%	14.3%	9.1%	8.9%	7.6%	6.1%
Charlson Comorbidity Index score						
1	66.4%	63.3%	62.4%	60.1%	55.1%	53.2%
2	20.7%	20.8%	21.9%	22.7%	25.3%	26.7%
≥3	12.9%	15.9%	15.7%	17.2%	19.6%	20.1%
Insurance type						
Medicaid	16.6%	17.8%	18.9%	19.3%	18.0%	17.2%
Medicare	28.1%	29.1%	30.3%	36.5%	40.3%	40.3%
Private	33.8%	30.3%	28.5%	29.2%	29.1%	29.5%
Uninsured	21.5%	22.8%	22.3%	15.0%	12.6%	13.0%

CM/PCS). Databases from 2016 to 2018 were coded using the Tenth Revision (ICD-10-CM/PCS). In the NIS, diagnoses are divided into two separate categories: principal diagnosis and secondary diagnoses. A principal diagnosis was the main ICD code for the hospitalization. Secondary diagnoses were any ICD code other than the principal diagnosis.

The study included NIS databases 2008, 2010, 2012, 2014, 2016, and 2018. These databases were searched for hospitalizations with the principal discharge diagnosis of DKA in patients with T1DM using ICD codes 25011, 25013, and E101. Records were excluded for patients <18 years, elective hospitalizations, and DKA in patients with type 2 or secondary diabetes mellitus. The biodemographic trends over time were highlighted. The total number of hospitalizations during each calendar year was obtained, and trends in inpatient mortality rate, mean length of hospital stay (LOS), and mean total hospital cost (THC) were calculated using multivariate logistic trend analysis. Total hospital cost was obtained using the HCUP Cost-to-Charge Ratio files and adjusted for inflation using the Medical Expenditure Panel Survey index for hospital care, with 2018 as the reference point.[4,5]

Stata Version 16 software (StataCorp, College Station, Texas) was used for data analysis. All analyses were conducted using the weighted samples for national estimates in accord with HCUP regulations for using the NIS database. Multivariate regression analysis was used to calculate the odds of trend in mortality, LOS, and THC following adjustment for age, sex, race, grouped Charlson Comorbidity Index (CCI), insurance type, mean household income, and hospital characteristics. All *P* values were two sided, with 0.05 set as the threshold for statistical significance. The NIS database lacks patient and hospital-level identifiers. This study, therefore, did not require approval of the Cook County Health institutional review board.

RESULTS

Between 2008 and 2018, there was a trend toward increasing hospitalizations for T1DM with DKA (*P*-trend <0.001), as shown in *Table 1* and *Figure 1*. The mean age over the period ranged from 34.2 to 36.1 years. About half of the hospitalizations were in women. Over the decade, there was a steady rise in the proportion of patients with a CCI >1, signifying increasing comorbidity burden in the population. There was a trend toward increasing use of Medicare as the insurance of patients. There was no statistically significant change in adjusted inpatient mortality in patients with DKA over the study period despite an apparent trend of a decreasing crude mortality rate (*P*-trend = 0.063).

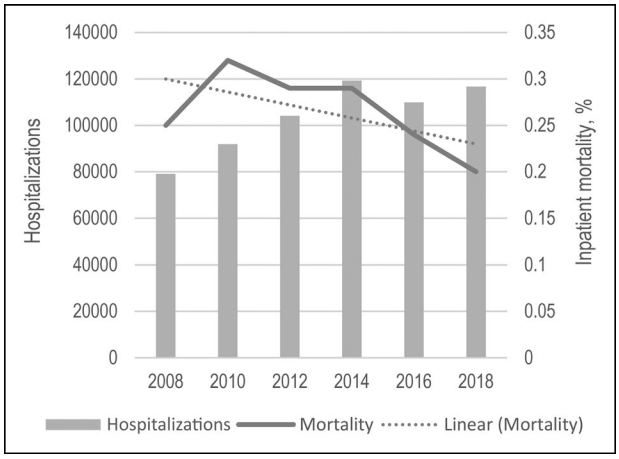

Figure 1. Trends in hospitalization for diabetic ketoacidosis in patients with type 1 diabetes mellitus. *P*-trend for mortality = 0.063.

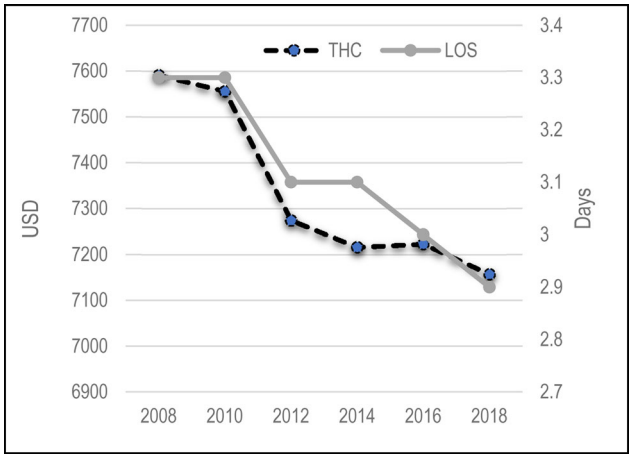

Figure 2. Health care cost utilization trend in hospitalizations for diabetic ketoacidosis. *P*-trend for length of stay (LOS) < 0.001; *P*-trend for total hospital costs (THC) < 0.001.

There was, however, a statistically significant decrease in both LOS and THC over the study period *(Table 2, Figure 2)*.

DISCUSSION

DKA is associated with high morbidity in patients with diabetes mellitus.[6] It is reported to be the presenting manifestation of diabetes in nearly 30% of patients with T1DM, and the incidence and economic burden of DKA have risen despite interventions.[7,8] Understanding DKA in T1DM patients is important in guiding future clinical practice. Between 2008 and 2018, there was a trend toward increasing hospitalizations for T1DM with DKA *(Table 1, Figure 1)*. The US Diabetes Surveillance System previously indicated an increase in hospitalization rates from 2009 to 2014, most notable in those <45 years old.[9] Although there was a trend toward increasing hospitalizations, there was no statistically significant change in adjusted inpatient mortality in patients with DKA over the study period, despite an apparent trend of a decreasing crude mortality rate. Previous reports have shown a decline in the case-fatality rate from 1.1% in 2009 to 0.4% in 2014.[9]

There are numerous possible explanations for the changes in hospitalizations, including lower thresholds for hospitalization.[9] There have been improvements in care because evidence-based recommendations have improved clinical outcomes.[8] Moreover, advances in diagnosis and inpatient care have helped reduce mortality.[7] Better understanding of the pathophysiology may also play a role in the reduced mortality.[9] Hospital admissions of less severe DKA cases may also result in increased hospitalizations without a rise in mortality.[9] Additionally, in 2009, the American Diabetes Association published a "euglycemic DKA" definition, defining it as metabolic acidosis, increased total body ketone concentration, and blood glucose levels ≤250 mg/dL. This is reported to account for about 10% of patients with DKA.[9,10] The expansion of the definition of DKA may also result in increased hospitalizations.

Hospitalizations may have risen secondary to medication nonadherence, which may be due to numerous factors, such as fear of weight gain, psychological distress, fear of hypoglycemia, and eating disorders.[11] Nonadherence may occur because of the rising cost of insulin, which tripled in price from 2003 to 2013.[7,11] New and improved insulin regimens have been developed, but these have also come at a higher cost.[7] Since medication nonadherence can lead to DKA, rising costs may contribute to increased hospitalizations.[1]

The rise in hospitalizations may also reflect a need for additional educational and follow-up strategies at earlier ages. DKA often occurs in patients with established disease; thus, interventions related to education and follow-up in those diagnosed with T1DM may help reduce future hospitalization rates.[9] In one study, a lower incidence of DKA at the time of diagnosis was noted when parents were made aware of the risks in their children, underscoring the effectiveness

Table 2. Outcomes for diabetic ketoacidosis in patients with type 1 diabetes mellitus

Outcome	2008	2010	2012	2014	2016	2018
Inpatient mortality	0.25%	0.32%	0.29%	0.29%	0.24%	0.20%
Mean length of stay (days)	3.3	3.3	3.1	3.1	3.0	2.9
Mean total hospital cost (USD)	7591	7556	7274	7216	7223	7157

of educational interventions.[12] Intensive screening and follow-up in patients with T1DM also resulted in reduced hospitalizations for DKA at diagnosis.[13] Previous studies' emphasis on the effectiveness on the aforementioned interventions may mean that additional investments in education and follow-up can reduce future hospitalization rates.

The CCI is a tool designed to predict 1-year mortality based on data from over 600 patients.[14] It has been adapted and modified for greater applicability.[15] The study also showed a steady rise in the proportion of patients with a CCI >1, signifying an increasing comorbidity burden in the population. Comorbidities are known to impact children with T1DM, with one study showing higher incidences of cardiovascular disease, mental disorders, epilepsy, obstructive pulmonary disease, and thyroid disease in children with T1DM.[16] Individuals with T1DM are at increased risk for eating disorders, depression, and anxiety.[17] The rise in CCI may be related to a rise in "double diabetes," or when patients with T1DM also develop features of metabolic syndrome.[18] A 2016 report identified double diabetes as an independent risk factor for macro- and microvascular comorbidities.[18] The potential rise in double diabetes may result in an increased comorbidity burden in patients and more comorbidities secondary to micro- and macrovascular damage.

There was a statistically significant decrease in both LOS and THC over the study period *(Table 2, Figure 2)*. This may reflect improvements in inpatient management in the time period included in our study. Previous studies reported that the use of standardized DKA treatments has led to reduced hospital LOS for DKA hospitalizations.[7] The decline in LOS and THC despite the rise in hospitalizations may reflect cost-effective care. Advancements in technology for the control of diabetes, such as subcutaneous insulin infusion and improved glucose monitoring, have not only led to improved glucose control but also reduced health care utilization, which may result in reduced overall costs. This underscores advancements that may lead to potentially less severe cases of DKA when patients are admitted.[7] Additionally, management of DKA in step-down units as opposed to intensive care units (ICUs) may lead to reduced costs. Data have shown no difference in in-hospital mortality, but significantly lower costs, in patients admitted to step-down units vs ICUs.[19] It should be noted that LOS may also be lower for other reasons, such as a potential decrease in overall hospital LOS during the study period, as evident in other medical disciplines, and the creation of evidence-based multidisciplinary care teams, computer decision support, hospital-wide education, and standardized order sets, which have been shown to improve overall care in DKA.[20,21]

As with any study, there are limitations that should be noted. Data from the NIS are subject to biases associated with retrospective studies. Moreover, the NIS reports information on hospitalizations rather than individual patients; thus, patients admitted numerous times would be included more than once in the data set. The NIS also does not include information about the severity of diagnosis at the time of admission. It uses ICD-10 codes to report hospitalizations, so it may have coding errors. Despite the aforementioned limitations, the demographics studied, large sample size, and analysis techniques make for a study that provides a current perspective on a major health care burden-causing disease while aiming to encourage further discourse and future controlled prospective studies on DKA hospitalizations in patients with T1DM.

In conclusion, the findings of this study reflect improvements in management, which may explain the decrease in mortality. The significant rise in hospitalizations may reflect a rise in T1DM or lack of treatment adherence or education regarding the importance of patient adherence. The drop in THC and LOS may reflect improvements in inpatient management secondary to standardized DKA interventions. Efforts to improve DKA care have not been futile, and continued focus on evidence-based interventions may improve future DKA management.

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